Non Technical Description

Cancer of the ovary is responsible for more than 12,000 deaths annually in the States. The disease is usually only diagnosed at a stage when the tumor has spread to invol structures in the abdominal cavity. The standard treatment for ovarian cancer involves surgic removal of the larger tumor masses combined with a combination of chemotherapy drug Although new chemotherapy drugs such as taxol are effective, complete responses are few, an toxicity is high. It therefore remains necessary to develop new treatment strategies to improve th survival and quality of life of patients who are afflicted with ovarian cancer.

The results of studies conducted in our laboratories and others have shown that particular cell type called the tumor infiltrating lymphocyte (TIL) can be isolated from th cancerous tumors that involve the lining of the abdominal cavity and the surface of the intestine. When these cells are removed from the body and are grown together with the patients tumor cel in tissue culture, along with a drug called recombinant interleukin-2 (rIL-2), the TILs wi frequently increase to larger numbers and develop an increased capacity to kill tumor cell obtained from the patient. rIL-2 is a protein substance that is almost identical to a natur substance that is found in the body and is produced in very small amounts by the cells of th body's immune system called lymphocytes. We are currently growing large numbers of TILs fo the experimental treatment of patients with advanced ovarian cancer in a clinical trial. This typ of treatment has been called adoptive cellular immunotherapy. In this trial we purify a particul type of TIL called "$CD8^+$ TIL" which appear to be responsible for the killing of tumor cells in tissu culture in certain cases.

This gene marker protocol will address an important scientific question: whether ovaria TIL-derived T cells that are expanded ex vivo in rIL-2 for intraperitoneal injection, concentra within metastatic tumors of the abdominal cavity. This information will be helpful in th development of improved therapies for ovarian cancer. In the past this type of question cou only be addressed by placing a radioactive label onto the cells and trying to trace the cells using gamma camera held over the patient. These techniques remain in use but are not sens specific enough to address the questions that are being posed.

Recently, use has been made of defective mouse viruses that have been genetically altere in the laboratory so that they are rendered incapable of multiplying in the patient. These virus have been used to transfer new genetic information into cells. The gene transfer approach being used to introduce a stable marker into cells that are being returned to the body for mark studies or in the development of new therapy approaches. Appropriate concerns have bee expressed regarding utilization of these defective viruses in patients. Marked improvements design and in quality control are contributing nevertheless, to safer and more efficient clinic applications.

In our study we intend to use the defective virus GINa, to transfer the gene for mark DNA. This marker gene is not present in human or mammalian cells. The gene encodes for a enzyme called neomycin phosphate transferase (NPT). The defective virus and related forms ha been used on a number of occasions to treat patients without reports of toxicity.

Patients who are enrolled in a study to be treated with TIL will be eligible for the marki protocol. During the growth of TIL in culture a bacterial "marker" gene will be inserted into portion of cultured TIL cells using a defective mouse retrovirus so that they can be traced aft reinjection into the patient. Following injections of a mixture of gene marked and unmark cells, samples of blood (about 10 cc each) and peritoneal fluid (approximately 100 cc) will obtained on days 4, 11, 18 and at one month after receiving the TIL injection. One month aft receiving the TIL, patient's will undergo a laparoscopy to evaluate their responses to t treatment. At this time biopsies will be obtained from tissues suspected of harboring canc Biopsies will also be obtained from certain normal tissues, e.g., peritoneum (lining of abdomir cavity) and lymph node (if easily accessible). These biopsies will be obtained to determine if t TIL have migrated into the tumor. This information might be useful for the development of futu treatment strategies in other patients with ovarian cancer. The laparoscopic surgery will performed to evaluate the response to the treatment and not for the marker study alone patients may receive the retrovirus modified cells.